Normal cellular response to chemoattractant signaling.

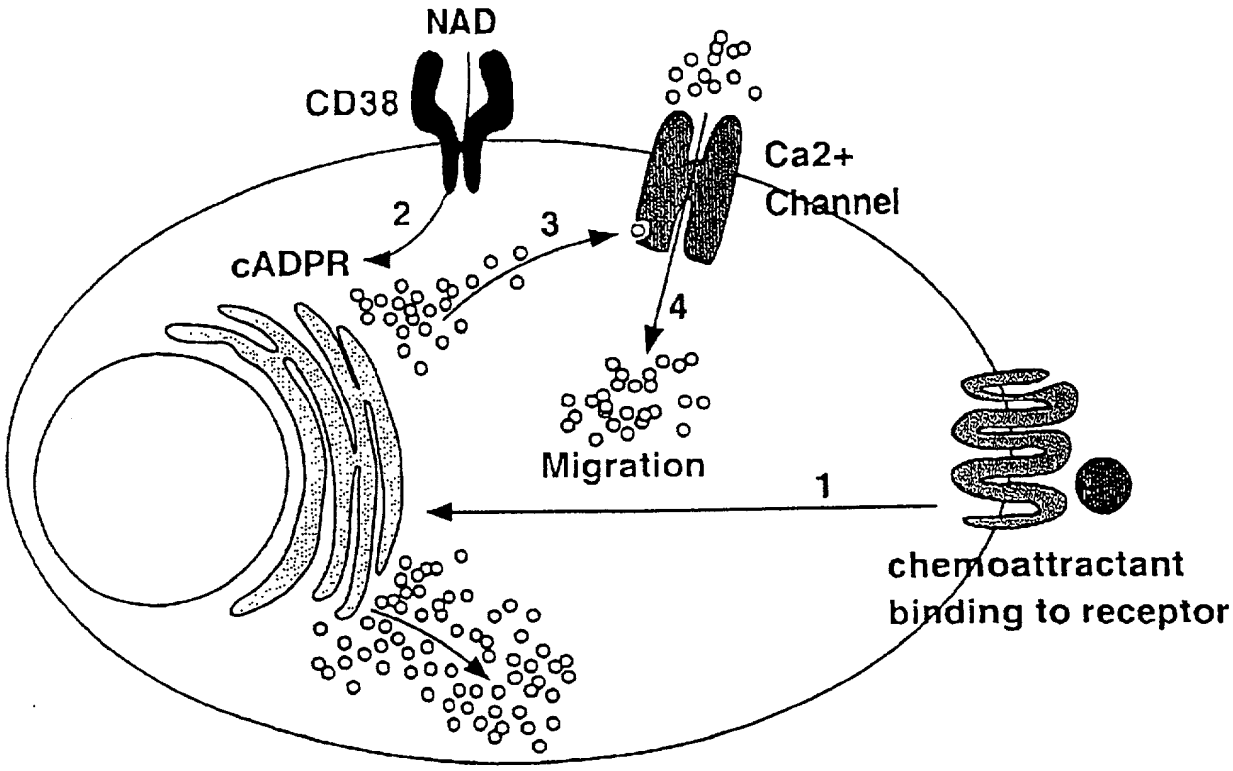

Figure 1

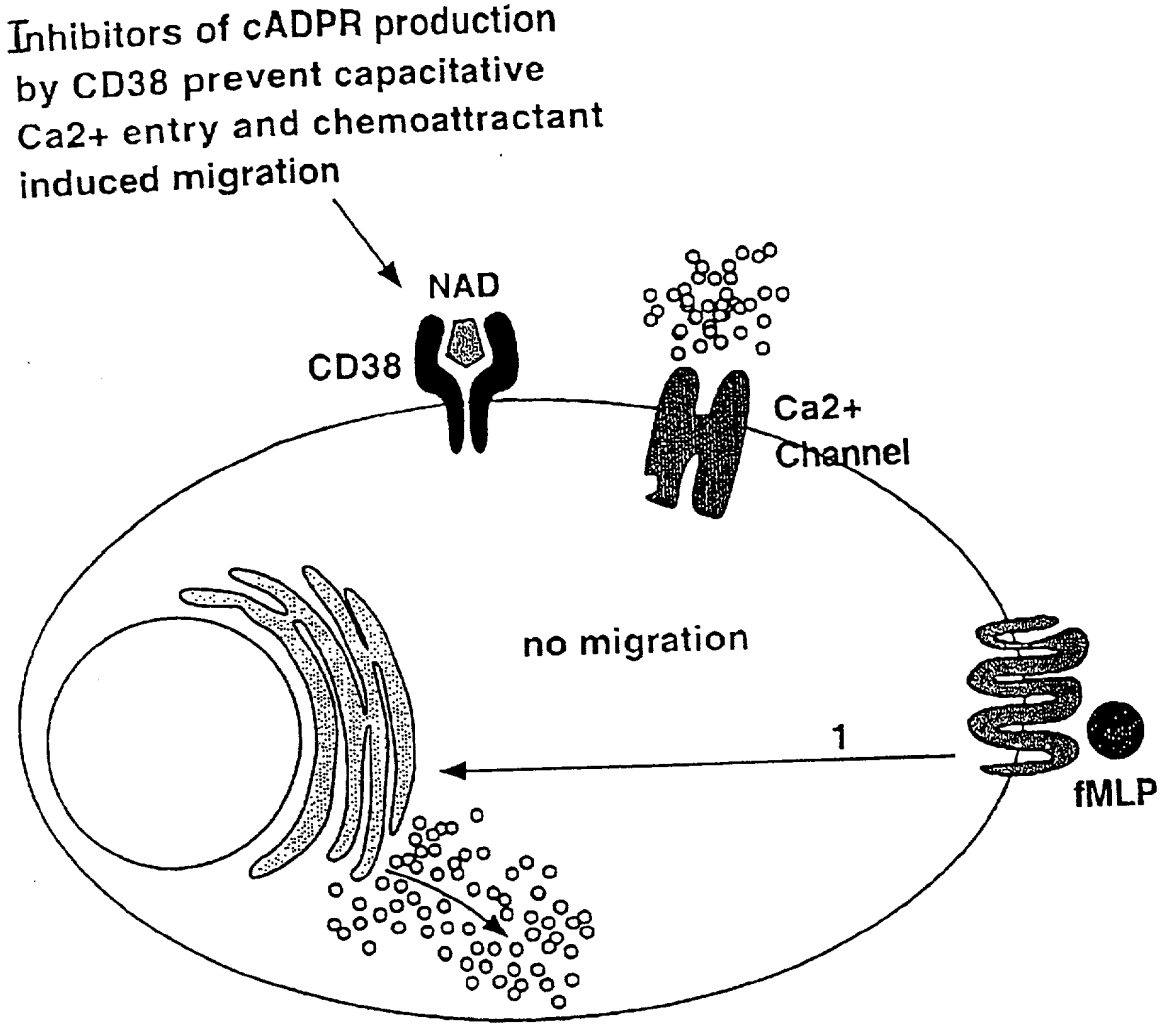
Inhibitors of cADPR production
by CD38 prevent capacitative
Ca2+ entry and chemoattractant
induced migration
NAD
CD38
Ca2+
Channel
no migration
1
fMLP

Figure 2

Proteins that regulate CD38 enzyme activity (screens will identify compounds that activate or inactivate these proteins)

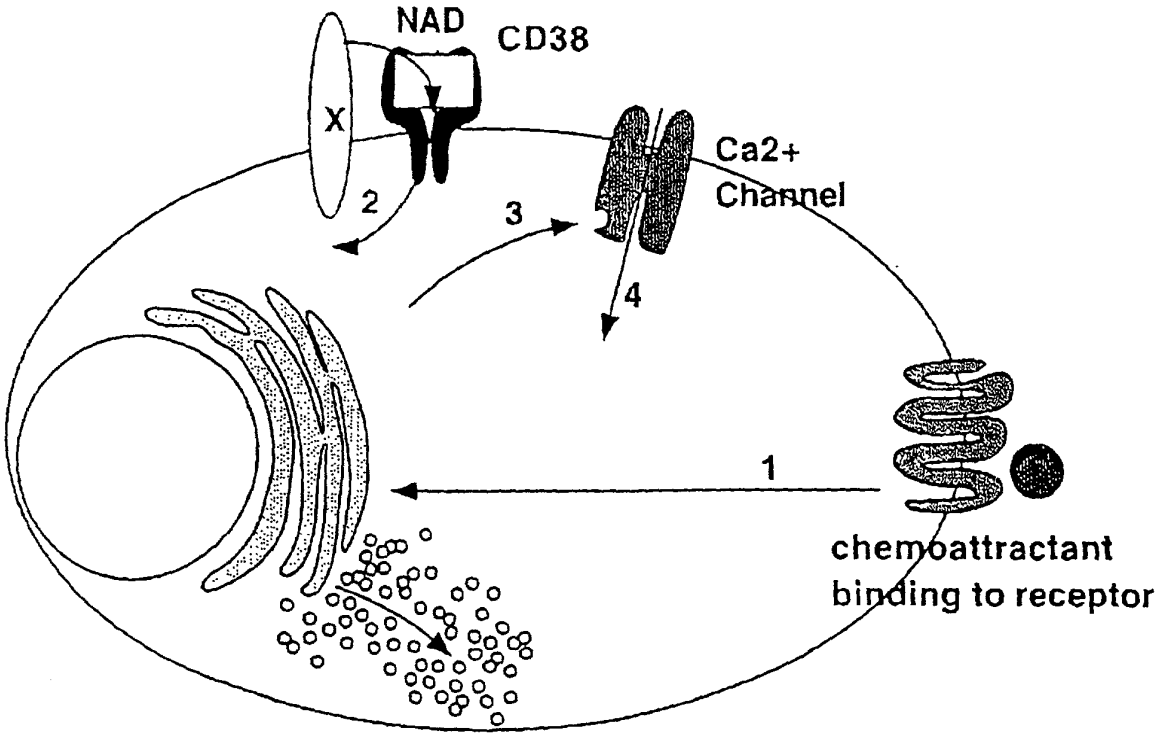

Figure 3

Proteins that regulate CD38 expression (screens will identify compounds that activate or inactivate these proteins)

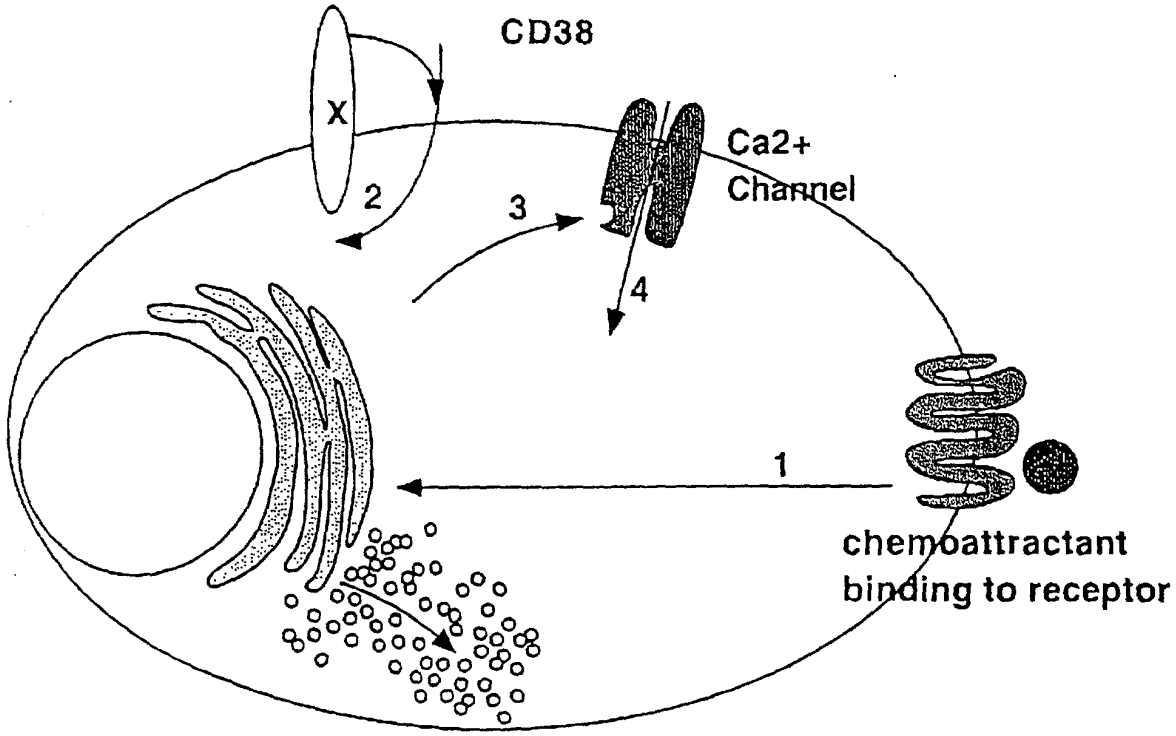

Figure 4

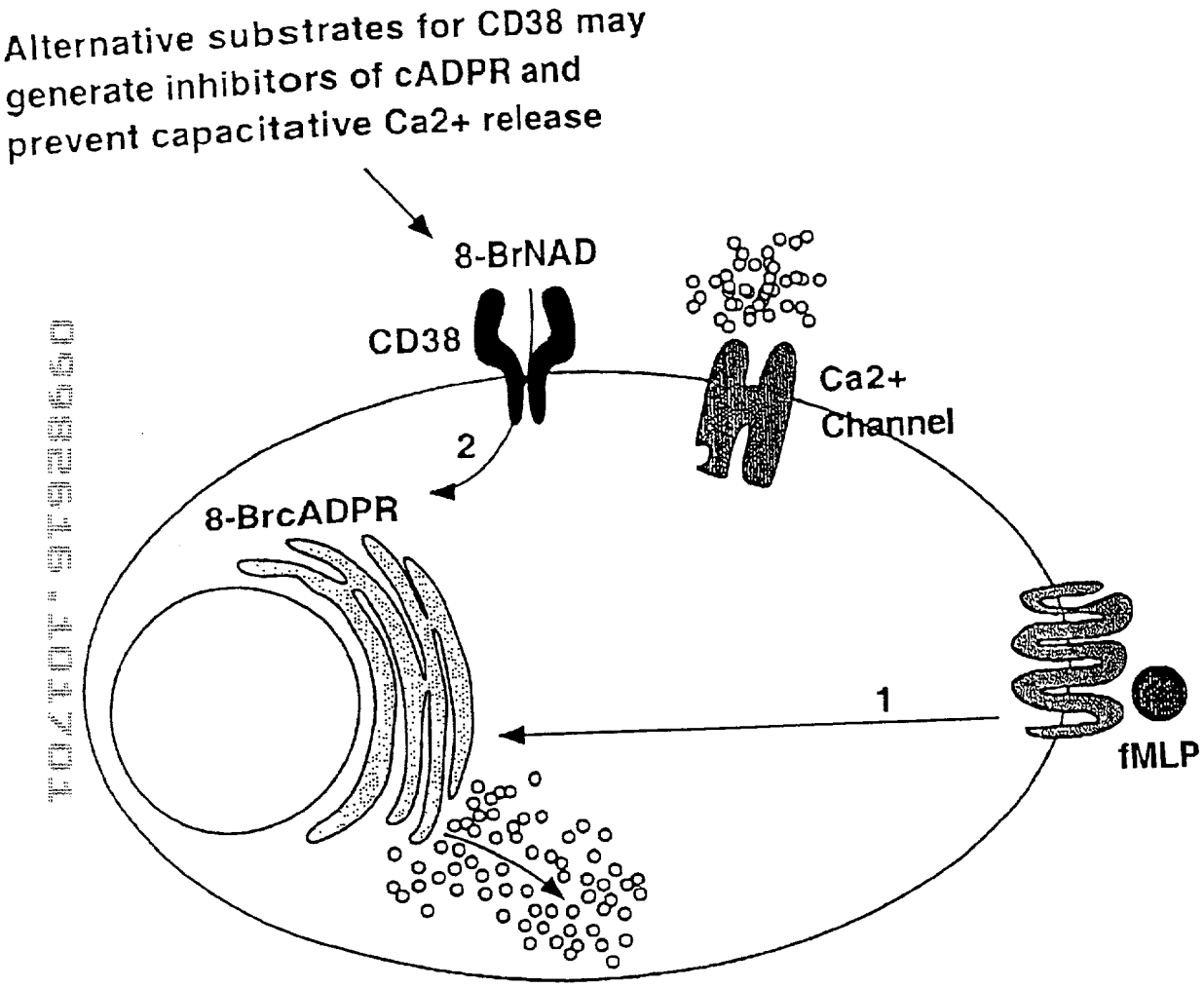
Alternative substrates for CD38 may generate inhibitors of cADPR and prevent capacitative Ca2+ release
8-BrNAD
CD38
Ca2+ Channel
2
8-BrcADPR
1
fMLP

Figure 5

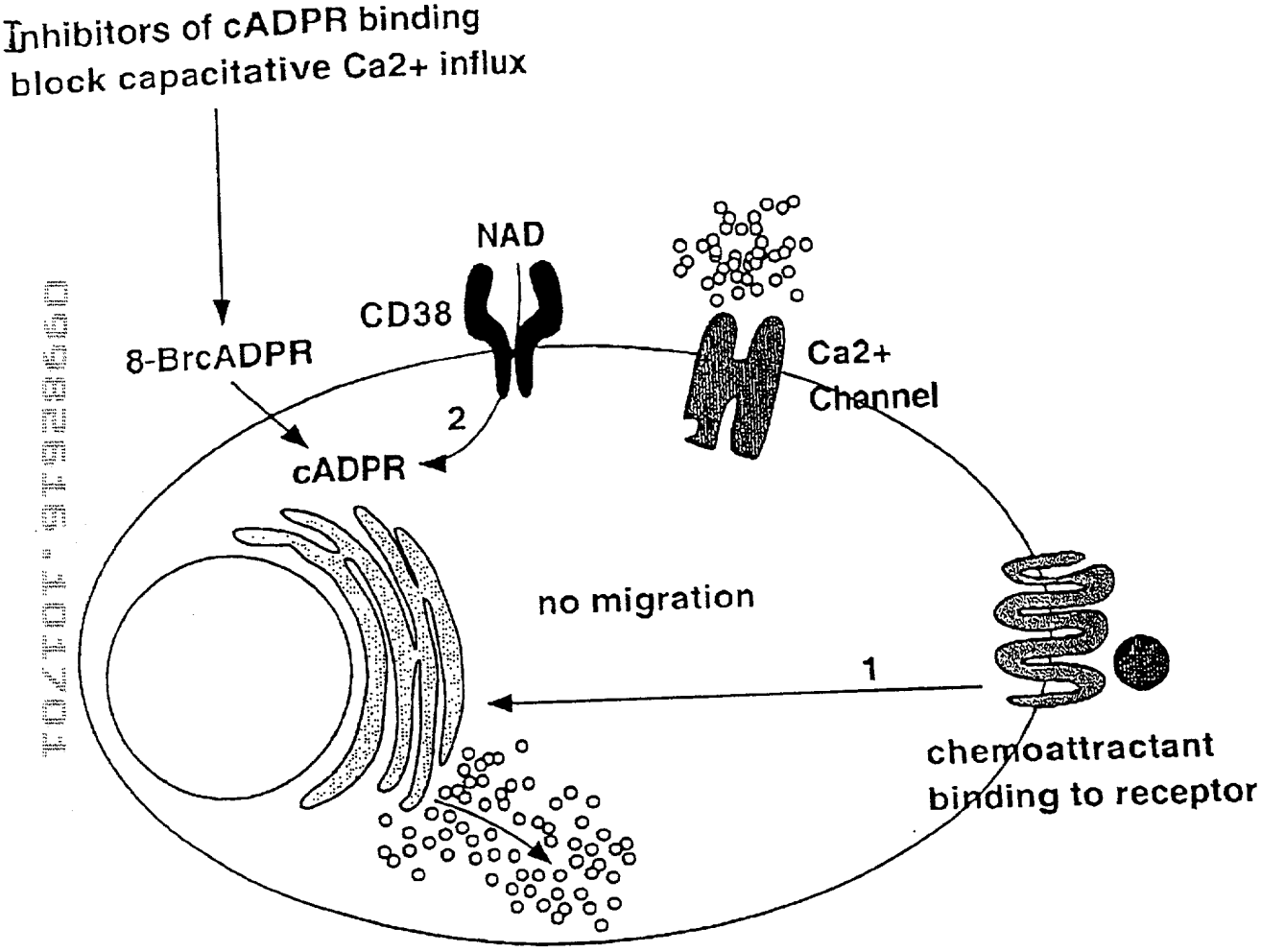
Inhibitors of cADPR binding
block capacitative Ca2+ influx
NAD
CD38
8-BrcADPR
Ca2+
Channel
2
cADPR
no migration
1
chemoattractant
binding to receptor

Figure 6

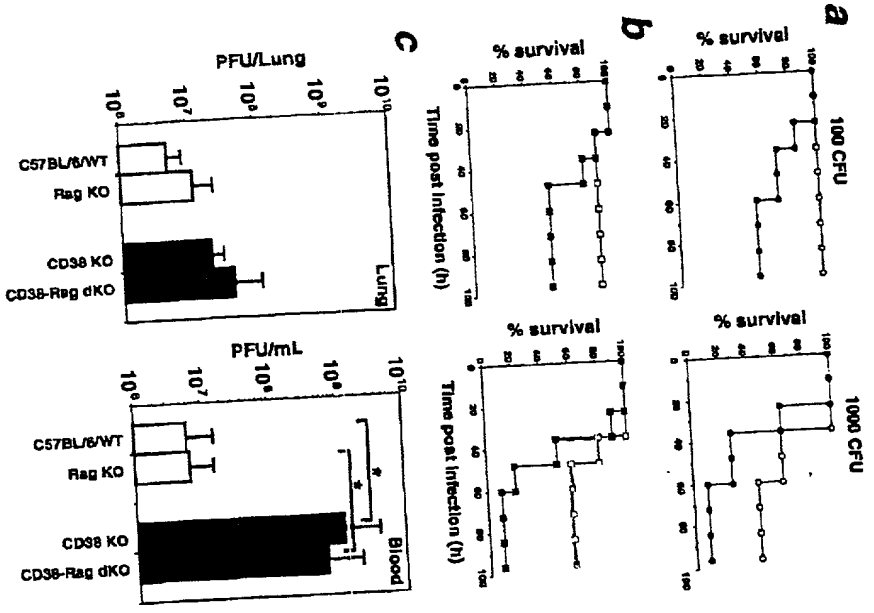
a
% survival
100 CFU
1000 CFU
Time post infection (h)
b
% survival
c
PFU/Lung
C57BL/6/WT
Rag KO
CD38 KO
CD38-Rag dKO
Lung
PFU/mL
Blood

Figure 7 A-C

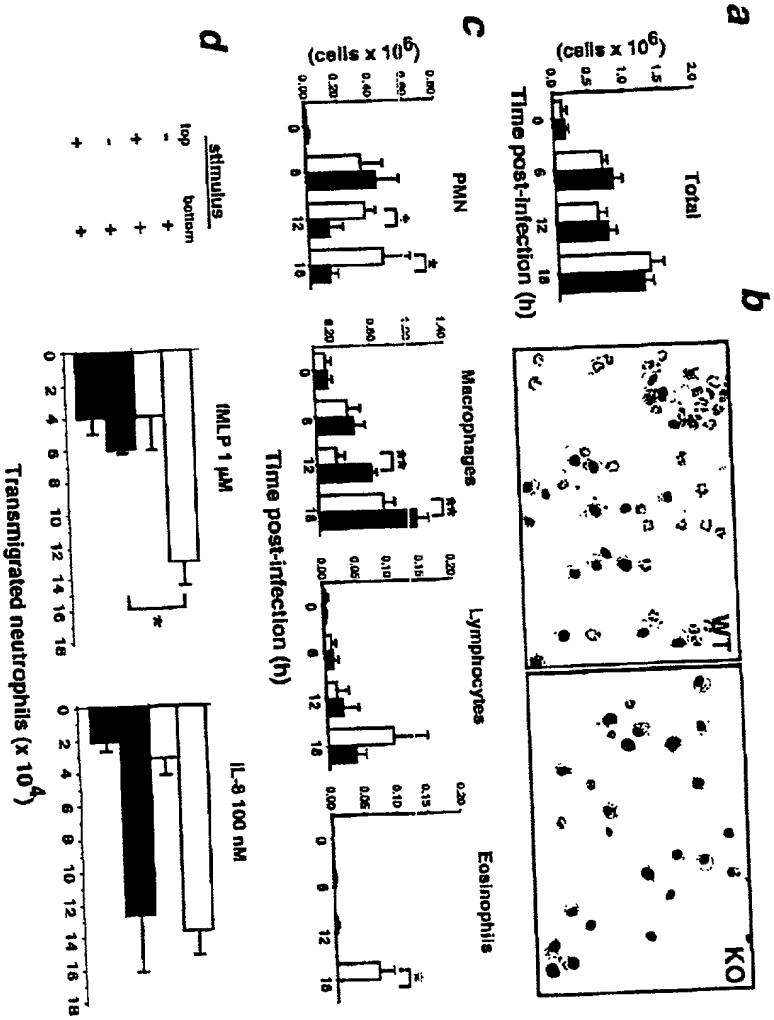
a
Total
(cells x 10^6)
Time post-infection (h)
b
WT
KO
c
PMN
Macrophages
Lymphocytes
Eosinophils
(cells x 10^6)
Time post-infection (h)
d
stimulus
top
bottom
fMLP 1 µM
IL-8 100 nM
Transmigrated neutrophils (x 10^4)

Figure 8 A-D

a
Bone Marrow
Peripheral Blood
Peritoneal Exudate
MAC-1
GR1
Relative cell number
CD38
Untreated
No Neutrophils
Thioglycollate treated
b
Human PMN
Rel. cell number
anti-CD38
c
RFU
Time (sec)
d
Brain
PMN
30 ng cDNA
60 ng cDNA
180 ng cDNA
no cDNA
1.8 pg cDNA
RyR3
220 bp
e
Digitonin 5μM
Ryanodine 1μM
+ Ruthenium Red
Ratio fluo-3/Fura red
Time (sec)
f
Digitonin 5μM
cADPR 100μM
+ 8-Br-cADPR
Time (sec)
g
Digitonin 5μM
Thapsigargin 1μM
+ 8-Br-cADPR
Time (sec)

Figure 9A-G

a
fMLP 1μM
WT
CD38KO
Ratio fluo-3/fura red
0 100 200 300 400 500
Time (sec)
IL-8 100 nM
WT
CD38KO
0 100 200 300 400 500
Time (sec)
b
fMLP 1μM
WT
CD38KO
Ratio fluo-3/fura red
0 100 200 300 400 500
Time (sec)
IL-8 100 nM
WT
CD38KO
0 100 200 300 400 500
Time (sec)
c
Pretreatment
none
8-Br-cADPR (25 μM)
8-Br-cADPR (100 μM)
fMLP 1μM
WT
CD38KO
Ratio fluo-3/fura red
0 100 200 300 400 500
Time (sec)
IL-8 100 nM
WT
CD38KO
0 100 200 300 400 500
Time (sec)
d
Pretreatment
none
EGTA (2mM)
8-Br-cADPR (25 μM)
8-Br-cADPR (100 μM)
fMLP 1μM
**
0 2 4 6 8 10 12
IL-8 100 nM
0 5 10 15 20 25
Transmigrated neutrophils (x 10⁴)

Figure 1b A-D

a
N(8-Br-A)D+ (500 µM)
fMLP 1µM
N(8-Br-A)D+
0 100 200 300 400 500
N(8-Br-A)D+ (1mM)
fMLP 1µM
N(8-Br-A)D+
0 100 200 300 400 600
Time (sec)
b
fMLP stimulated
WT
CD38KO
*
Transmigrated neutrophils
(x 10⁴)
0 4 8 12 16
c
IL-8 stimulated
WT
CD38KO
Transmigrated neutrophils
(x 10⁴)
0 4 8 12 16

Figure 11A-C

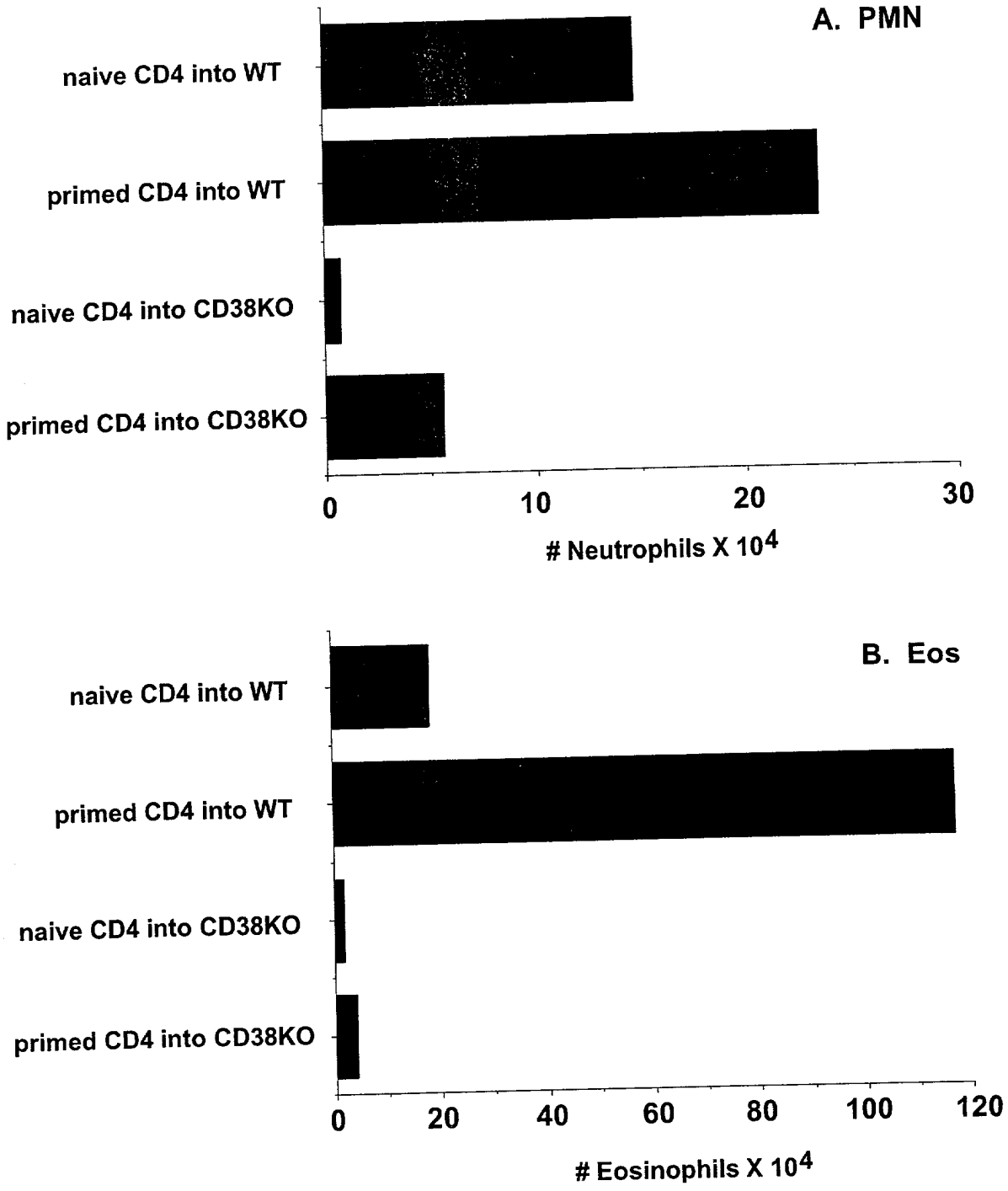
A. PMN
naive CD4 into WT
primed CD4 into WT
naive CD4 into CD38KO
primed CD4 into CD38KO
0
10
20
30
Neutrophils X 10^4
B. Eos
naive CD4 into WT
primed CD4 into WT
naive CD4 into CD38KO
primed CD4 into CD38KO
0
20
40
60
80
100
120
Eosinophils X 10^4

Figure 12

Figure 13A

```
Consensus            GGAAAGAACG TAGACATATA TTGTTATATA GATTTGTTCA GTTATTTTTC    50
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 GGAAAGAACG TAGACATATA TTGTTATATA GATTTGTTCA GTTATTTTTC    50

Consensus            ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA   100
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA   100

Consensus            TCAAATATTT TTGTCTTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG   150
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 TCAAATATTT TTGTCTTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG   150

Consensus            TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA   200
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA   200

Consensus            CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTTGAAAG CATTTTACTT   250
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTTGAAAG CATTTTACTT   250

Consensus            TCAACTCATA CTAAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA   300
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 TCAACTCATA CTAAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA   300

Consensus            TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC   350
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC   350

Consensus            ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT   400
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------
SM38                 ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT   400

Consensus            CGTGGAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACTACATT   450
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- -GGAGTATGT CGTTCTCTAG AAACTACATT    29
SM38                 CGTGGAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACTACATT   450
```

Figure 13B

```
Consensus            TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAACAG   500
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           TCCAGGATAT CTGTTTGATG AATTGAATTG GTGCAATGGC AGTTTAACAG    79
SM38                 TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAACAG   500

Consensus            GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT   550
EST AW017229 comp    ---------- ---------- ---------- ---------- ----------
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT   129
SM38                 GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT   550

Consensus            GTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC   600
EST AW017229 comp    ---------- ---------- ------GGCT GAGTATGCCA GGAGAGCATC    24
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           GTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC   179
SM38                 GTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC   600

Consensus            TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG   650
EST AW017229 comp    TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG    74
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG   229
SM38                 TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG   650

Consensus            AAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG   700
EST AW017229 comp    AAAATAAAAC TTTTGGAAAA ATAGAACTAC CATT-GTTAA AACATCCTCG   123
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           AAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG   279
SM38                 AAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTG-TTAA AACATCCTCG   699

Consensus            AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA   750
EST AW017229 comp    AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA   173
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           A--------- ---------- ---------- ---------- ----------   280
SM38                 AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA   749

Consensus            ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG   800
EST AW017229 comp    ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG   223
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------   280
SM38                 ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG   799

Consensus            AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG   850
EST AW017229 comp    AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG   273
EST AI067047 comp    ---------- ---------- ---------- ---------- ----------
EST N20756           ---------- ---------- ---------- ---------- ----------   280
SM38                 AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG   849

Consensus            ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG   900
EST AW017229 comp    ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG   323
EST AI067047 comp    ---------- ---ATTGAAA ATCATGGCAA ACAACTATGT CAGTTTTCAG    37
EST N20756           ---------- ---------- ---------- ---------- ----------   280
SM38                 ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG   899
```

Figure 13C

```
Consensus                CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC   950
EST AW017229 comp        CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC   373
EST AI067047 comp        CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC    87
EST N20756               ---------- ---------- ---------- ---------- ----------   280
SM38                     CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTTT TCCGCTAGTC   949

Consensus                ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT  1000
EST AW017229 comp        ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT   423
EST AI067047 comp        ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT   137
EST N20756               ---------- ---------- ---------- ---------- ----------   280
SM38                     ATTTGTTTAA CTTTTTATAC TTCCATGAAT TGAAATAACT TTTCAGAACT   999

Consensus                AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGMCATTA  1050
EST AW017229 comp        AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGCCATTA   473
EST AI067047 comp        AAACTTTG-- ---------- ---------- ---------- ----------   145
EST N20756               ---------- ---------- ---------- ---------- ----------   280
SM38                     AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGACATTA  1049
```

Figure 14

```
GGAAAGAACGTAGACATATATTGTTATATAGATTTGTTCAGTTATTTTTCACAATCTTTTAATTCAAATA    70
 E  R  T  .  T  Y  I  V  I  .  I  C  S  V  I  F  H  N  L  L  I  Q  I

ATGATGAACGTAATATTGTTTCTTACTTTATCAAATATTTTTGTCTTTAACTCTGCACAACATCAAATAA   140
 M  M  N  V  I  L  F  L  T  L  S  N  I  F  V  F  N  S  A  Q  H  Q  I

ACTTACTTAGTGAAATAGTACAATCACGATGTACTCAGTGGAAGGTTGAACATGGAGCTACTAATATAAG   210
N  L  L  S  E  I  V  Q  S  R  C  T  Q  W  K  V  E  H  G  A  T  N  I  S

TTGTAGTGAGATCTGGAATTCATTTGAAAGCATTTTACTTTCAACTCATACTAAATCAGCATGTGTTATG   280
 C  S  E  I  W  N  S  F  E  S  I  L  L  S  T  H  T  K  S  A  C  V  M

AAATCAGGGTTATTCGATGATTTTGTTTATCAATTGTTTGAATTGGAACAACAACAACAACAGCGACACC   350
 K  S  G  L  F  D  D  F  V  Y  Q  L  F  E  L  E  Q  Q  Q  Q  Q  R  H

ACACAATTCAAACGGAACAATACTTCCATTCTCAAGTGATGAACATCATTCGTGGAATGTGTAAACGTCT   420
H  T  I  Q  T  E  Q  Y  F  H  S  Q  V  M  N  I  I  R  G  M  C  K  R  L

TGGAGTATGTCGTTCTCTAGAAACTACATTTCCAGGATATCTGTTTGATGAATTGAATTGGTGTAATGGC   490
 G  V  C  R  S  L  E  T  T  F  P  G  Y  L  F  D  E  L  N  W  C  N  G

AGTTTAACAGGCAACACAAAATACGGGACTGTATGTGGATGCGATTATAAAAGTAATGTTGTTCATGCGT   560
 S  L  T  G  N  T  K  Y  G  T  V  C  G  C  D  Y  K  S  N  V  V  H  A

TCTGGCAAAGTGCTTCGGCTGAGTATGCCAGGAGAGCATCTGGTAACATCTTTGTGGTACTGAATGGCTC   630
F  W  Q  S  A  S  A  E  Y  A  R  R  A  S  G  N  I  F  V  V  L  N  G  S

GGTCAAAGCTCCATTTAATGAAAATAAAACTTTTGGAAAAATAGAACTACCATTGTTAAAACATCCTCGA   700
 V  K  A  P  F  N  E  N  K  T  F  G  K  I  E  L  P  L  L  K  H  P  R

GTACAACAATTAACAGTGAAATTAGTTCATAGTTTGGAAGATGTAAATAACCGACAAACATGTGAATCGT   770
 V  Q  Q  L  T  V  K  L  V  H  S  L  E  D  V  N  N  R  Q  T  C  E  S

GGAGTCTGCAAGAACTTGCAAACAAGCTGAACTCTGTACATATTCCTTTTCGTTGCATTGACGATCCTTT   840
W  S  L  Q  E  L  A  N  K  L  N  S  V  H  I  P  F  R  C  I  D  D  P  L

AGAGTTCAGACATTATCAATGCATTGAAAATCCTGGCAAACAACTATGTCAGTTTTCAGCTTCGACGAGG   910
 E  F  R  H  Y  Q  C  I  E  N  P  G  K  Q  L  C  Q  F  S  A  S  T  R

TCAAACGTCGAGACATTACTCATACTTTTTCCGCTAGTCATTTGTTTAACTTTTTATACTTCCATGAATT   980
 S  N  V  E  T  L  L  I  L  F  P  L  V  I  C  L  T  F  Y  T  S  M  N

GAAATAACTTTTCAGAACTAAACTTTGAACAGAGAAAGAGAACAATGATAATAAAGGAATAGGACATTAA   1050
.  N  N  F  S  E  L  N  F  E  Q  R  K  R  T  M  I  I  K  E  .  D  I  N

TGAAAAAAAAAAAAAAAAAAAAA   1073
 E  K  K  K  K  K  K
```

Figure 15 A-B

A.

```
Consensus       M......... .L.......S ....I..... L......RC. ..........     50

Aplysia cd38p   MSPVAIVACV CLAVTLTRIS PSEAIFPTPE LQNVFLGRCK DYEITRYLTI     50
SM38p           M--MNVILFL TLSNIFVFNS AQHQI---NL LSEIVQSRCT QWKVEH----     41

Consensus       .......C.. .W..F..... ....K..C.. ..G...DF.. ..........    100

Aplysia cd38p   LPRVKSDCRA LWTNFFKAFS F---KAPCNL DLGSYKDFFQ RAQQTLPKNK     97
SM38p           -GATNISCSE IWNSFESILL STHTKSACVM KSGLFDDFVY QLFELEQQQQ     90

                                                  *
Consensus       .......... .......... .......... ..LE.T.PGY ....L.WC..    150

Aplysia cd38p   VMFWSGVYDE --AHDF---- ADDGRKYI-- -TLEDTLPGY MLNSLVWCGQ    138
SM38p           QRHHTIQTEQ YFHSQVMNII RGMCKRLGVC RSLETTFPGY LFDELNWCNG    140

Consensus       .......... VC....D... .....FW..A S..YA..A.G .......GS.    200

Aplysia cd38p   RDKPGFNQK- VCPDFKDCPV QARESFWGTA SSSYAHSAEG DVTYMVDGSN    187
SM38p           SLTGNTKYGT VC--GCDYKS NVVHAFWQSA SAEYARRASG NIFVVLNGS-    186

                              *
Consensus       .......... .FGK.ELP.L ....V..... ...H.L.... ....C...SL    250

Aplysia cd38p   PKVPAYRPDS FFGKYELPNL TNK-VTKVKV IVLHQLGQKI I-ERCGAGSL    235
SM38p           -VKAPFNENK TFGKIELPLL KHPRVQQLTV KLVHSLEDVN NRQTCESWSL    236

Consensus       ..L....... ...F.C...P .......C.. NP....CQ.. ..........    300

Aplysia cd38p   LDLEMVVKAK KFGFDCVENP KSVLFLLCAD NPNARECQLA KRYYRIA---    282
SM38p           QELANKLNSV HIPFRCIDDP LEFRHYQCIE NPGKQLCQFS ASTRSNVETL    286

Consensus       .......... .......                                       317

Aplysia cd38p   ---------- -------                                       282
SM38p           LILFPLVICL TFYTSMN                                       303
```

B.

```
Consensus       M......... .......... .......... ...IL...L. ........Q.     50

Human CD38      MANCEFSPVS GDKPCCRLSR RAQLCLGVSI LVLILVVVLA VVVPRWRQQW     50
SM38p           M--------- ---------- ---------- MNVILFLTLS NIFVFNSAQ-     20

Consensus       .......... E.V..RC... .......... .C...W..F. ....S.H.K.    100

Human CD38      SGPGTTKRFP ETVLARCVKY TEIHPEMRHV DCQSVWDAFK GAFIS---KH     97
SM38p           ---HQINLLS EIVQSRCTQW -KVEHGATNI SCSEIWNSFE SILLSTHTKS     66

Consensus       .C........ ...YQ..... .......... .......S.. ..........    150

Human CD38      PCNITEED-- ---YQPLMKL GTQTVPCNKI L----LWSRI KDLAHQFTQV    138
SM38p           ACVMKSGLFD DFVYQLFELE QQQQQRHHTI QTEQYFHSQV MNIIRGMCKR    116

                      *
Consensus       ......LE.T ..GYL.D.L. WC....T... .Y...C.... ..C....N.V    200

Human CD38      QRDMFTLEDT LLGYLADDLT WCGEFNTSKI NYQS-CPDWR KDC--SNNPV    185
SM38p           LGVCRSLETT FPGYLFDELN WCNGSLTGNT KYGTVCG--- --CDYKSNVV    161

                                                  *
Consensus       ..FW...S.. .A..A..... V.LNGS.... F..N.TFG.. E...L....V    250

Human CD38      SVFWKTVSRR FAEAACDVVH VMLNGSRSKI FDKNSTFGSV EVHNLQPEKV    235
SM38p           HAFWQSASAE YARRASGNIF VVLNGSVKAP FNENKTFGKI ELPLLKHPRV    211

Consensus       Q.L.....H. ......R..C ......EL.. ......I.F. C.........    300

Human CD38      QTLEAWVIHG GRE-DSRDLC QDPTIKELES IISKRNIQFS CKNIYRPDKF    284
SM38p           QQLTVKLVHS LEDVNNRQTC ESWSLQELAN KLNSVHIPFR CIDDPLEFRH    261

Consensus       .QC..NP... .C........ .......... ........TS ..            342

Human CD38      LQCVKNPEDS SC-------- ---------- --------TS EI            300
SM38p           YQCIENPGKQ LCQFSASTRS NVETLLILFP LVICLTFYTS MN            303
```

```
MMNVILFLTL SNIFVFNSAQ HQINLLSEIV QSRCTQWKVE HGATNISCSE    50
IWNSFESILL STHTKSACVM KSGLFDDFVY QLFELEQQQQ QRHHTIQTEQ   100
YFHSQVMNII RGMCKRLGVC RSLETTFPGY LFDELNWCNG SLTGNTKYGT   150
VCGCDYKSNV VHAFWQSASA EYARRASGNI FVVLNGSVKA PFNENKTFGK   200
IELPLLKHPR VQQLTVKLVH SLEDVNNRQT CESWSLQELA NKLNSVHIPF   250
RCIDDPLEFR HYQCIENPGK QLCQFSASTR SNVETLLILF PLVICLTFYT   300
SMN                                                      303
```


Figure 16

ATGATGAAYG TNATHYTNTT YYTNACNYTN WSNAAYATHT TYGTNTTYAA 50
YWSNGCNCAR CAYCARATHA AYYTNYTNWS NGARATHGTN CARWSNMGNT 100
GYACNCARTG GAARGTNGAR CAYGGNGCNA CNAAYATHWS NTGYWSNGAR 150
ATHTGGAAYW SNTTYGARWS NATHYTNYTN WSNACNCAYA CNAARWSNGC 200
NTGYGTNATG AARWSNGGNY TNTTYGAYGA YTTYGTNTAY CARYTNTTYG 250
ARYTNGARCA RCARCARCAR CARMGNCAYC AYACNATHCA RACNGARCAR 300
TAYTTYCAYW SNCARGTNAT GAAYATHATH MGNGGNATGT GYAARMGNYT 350
NGGNGTNTGY MGNWSNYTNG ARACNACNTT YCCNGGNTAY YTNTTYGAYG 400
ARYTNAAYTG GTGYAAYGGN WSNYTNACNG GNAAYACNAA RTAYGGNACN 450
GTNTGYGGNT GYGAYTAYAA RWSNAAYGTN GTNCAYGCNT TYTGGCARWS 500
NGCNWSNGCN GARTAYGCNM GNMGNGCNWS NGGNAAYATH TTYGTNGTNY 550
TNAAYGGNWS NGTNAARGCN CCNTTYAAYG ARAAYAARAC NTTYGGNAAR 600
ATHGARYTNC CNYTNYTNAA RCAYCCNMGN GTNCARCARY TNACNGTNAA 650
RYTNGTNCAY WSNYTNGARG AYGTNAAYAA YMGNCARACN TGYGARWSNT 700
GGWSNYTNCA RGARYTNGCN AAYAARYTNA AYWSNGTNCA YATHCCNTTY 750
MGNTGYATHG AYGAYCCNYT NGARTTYMGN CAYTAYCART GYATHGARAA 800
YCCNGGNAAR CARYTNTGYC ARTTYWSNGC NWSNACNMGN WSNAAYGTNG 850
ARACNYTNYT NATHYTNTTY CCNYTNGTNA THTGYYTNAC NTTYTAYACN 900
WSNATGAAY 909

Figure 17